

CLAIMS

We Claim:

1. A compound of formula I

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I

its enantiomeric, diastomeric or tautomeric isomer, or a pharmaceutically acceptable salt thereof wherein,

10 R^1 is

- (a) Cl,
- (b) Br,
- (c) F, or
- (d) CN;

15 R^2 is

- (a) C_{1-4} alkyl optionally substituted by one or more OH or C_{1-4} alkoxy, or
- (b) $(CH_2)_mOCH_2CH_2OH$;

R^3 is C_{1-2} alkyl;

R^4 is phenyl optionally fused to a benzene or pyridine ring, and optionally substituted

20 with one or more R^6 ;

R^5 is

- (a) H, or
- (b) C_{1-2} alkyl optionally substituted by OH;

R^6 is

- 25 (a) halo,
- (b) OCF_3 ,
- (c) cyano,
- (d) nitro,
- (e) $CONR^7R^8$,
- 30 (f) NR^7R^8 ,
- (g) C_{1-7} alkyl, which is optionally partially unsaturated and is optionally substituted by one or more R^9 ,
- (h) $O(CH_2CH_2O)_nR^{10}$,

- (i) OR^{10} ,
 - (j) CO_2R^{10} ,
 - (k) phenyl optionally substituted by halo, C_{1-7} alkyl, or C_{1-7} alkoxy;
 - (l) SR^{10} ,
 - 5 (m) imidazolyl,
 - (n) $S(O)_mNR^7R^8$,
 - (o) $NHC(=O)R^{10}$, or
 - (p) any two adjacent R^6 substituents taken together constitute a group of the formula $-O(CH_2)_mO-$, $-(NH)(CO)(CH_2)_jO-$, or $-(CH_2)_i-$;
- 10 R^7 and R^8 are independently
- (a) H,
 - (b) phenyl optionally substituted by halo, C_{1-7} alkyl, or C_{1-7} alkoxy,
 - (c) C_{1-7} alkyl which is optionally substituted by one or more OR^{10} , phenyl, or halo substituents,
 - 15 (d) C_{3-8} cycloalkyl,
 - (e) $(C=O)R^{11}$, or
 - (f) R^7 and R^8 together with the nitrogen to which they are attached form a het, wherein het is a five- (5), or six- (6) membered heterocyclic ring having one (1), two (2), or three (3) heteroatoms selected from the group consisting of oxygen, sulfur,
 - 20 or nitrogen, wherein het is optionally substituted with C_{1-4} alkyl;
- R^9 is
- (a) oxo,
 - (b) phenyl optionally substituted by halo, C_{1-7} alkyl, or C_{1-7} alkoxy,
 - (c) OR^{10} ,
 - 25 (d) $O(CH_2CH_2)OR^{10}$,
 - (e) SR^{10} ,
 - (f) NR^7R^8 ,
 - (g) halo,
 - (h) CO_2R^{10} ,
 - 30 (i) $CONR^{10}R^{10}$, or
 - (j) C_{3-8} cycloalkyl optionally substituted by OR^{10} ;
- R^{10} is
- (a) H,

- (b) C₁₋₇alkyl,
- (c) C₃₋₈cycloalkyl, or
- (d) phenyl optionally substituted by halo, C₁₋₇alkyl, or C₁₋₇alkoxy;

R¹¹ is

- (a) C₁₋₇alkyl,
- (b) C₃₋₈cycloalkyl, or
- (c) phenyl optionally substituted by halo, C₁₋₇alkyl, or C₁₋₇alkoxy;

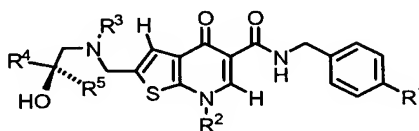
i is 3 or 4;

j is 0 or 1;

- n is 1, 2, 3, 4 or 5; and

each m is independently 1 or 2.

- 2. A compound of claim 1 which is a compound of formula IA



IA.

- 3. A compound of claim 1 or 2 wherein R¹ is chloro.
- 4. A compound of claim 1 or 2 wherein R² is C₁₋₃alkyl.
- 5. A compound of claim 1 or 2 wherein R² is methyl.
- 6. A compound of claim 1 or 2 wherein R² is ethyl or *n*-propyl.
- 7. A compound of claim 1 or 2 wherein R² is C₁₋₃alkyl substituted with one or two hydroxy.
- 8. A compound of claim 1 or 2 wherein R² is 2-hydroxyethyl, 3-hydroxypropyl, or 2,3-dihydroxypropyl.
- 9. A compound of claim 1 or 2 wherein R² is C₁₋₄alkyl substituted by C₁₋₄alkoxy.

10. A compound of claim 1 or 2 wherein R^2 is C_{1-4} alkyl substituted by methoxy.
11. A compound of claim 1 or 2 wherein R^2 is 2-methoxyethyl.
- 5 12. A compound of claim 1 or 2 wherein R^3 is methyl.
13. A compound of claim 1 or 2 wherein R^3 is ethyl.
- 10 14. A compound of claim 1 or 2 wherein R^4 is phenyl.
15. A compound of claim 1 or 2 wherein R^4 is phenyl substituted by R^6 .
16. A compound of claim 1 or 2 wherein R^4 is naphthyl, optionally substituted with
15 one or more R^6 .
17. A compound of claim 1 or 2 wherein R^4 is phenyl, fused to a pyridine ring,
optionally substituted with one or more R^6 .
- 20 18. A compound of claim 15 wherein R^6 is OH, halo, C_{1-4} alkyl, C_{1-4} alkoxy, cyano,
nitro, OCF_3 , NR^7R^8 , phenyl, or $CONR^7R^8$.
19. A compound of claim 15 wherein R^6 is OH, methoxy, or cyano.
- 25 20. A compound of claim 18 wherein R^7 and R^8 together with the nitrogen to
which they are attached form a het, wherein het is morpholine, piperidine, piperazine,
or pyrrolidine.
21. A compound of claim 1 or 2 wherein R^5 is hydrogen.
- 30 22. A compound of claim 1 or 2 wherein R^5 is methyl or ethyl.

23. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

24. A method of treating infections by herpesviruses which comprises
5 administering to a mammal in need thereof a compound of claim 1.

25. The method of claim 24 wherein said herpesviruses is herpes simplex virus types 1, herpes simplex virus types 2, varicella zoster virus, human cytomegalovirus, Epstein-Barr virus, human herpes virus 6, human herpes virus 7 or human herpes virus
10 8.

26. The method of claim 25 wherein said herpesviruses is human cytomegalovirus.

27. The method of claim 25 wherein said herpesviruses is varicella zoster virus or
15 Epstein-Barr virus.

28. The method of claim 25 wherein said herpesviruses is herpes simplex virus types 1 or herpes simplex virus types 2.

20 29. The method of claim 24 wherein the compound of claim 1 is administered orally, parenterally or topically.

30. The method of claim 24 wherein the compound of claim 1 is in an amount of from about 0.1 to about 300 mg/kg of body weight.
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31. The method of claim 24 wherein the compound of claim 1 is in an amount of from about 1 to about 30 mg/kg of body weight.

32. The method of claim 24 wherein said mammal is a human.
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33. The method of claim 24 wherein said mammal is an animal.

34. A method of treating atherosclerosis and restenosis comprising administering to a mammal in need thereof a compound of claim 1 or 2.

35. A method for inhibiting a herpesviral DNA polymerase, comprising contacting
5 the polymerase with an effective inhibitory amount of a compound of claim 1.

36. A compound of claim 1, or a pharmaceutically acceptable salt thereof, for use in the manufacture of medicines for the treatment or prevention of a herpesviral infection in a mammal.

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37. A compound of claim 1 which is

(1) *N*-(4-chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-(4-hydroxyphenyl)ethyl)(methyl)-amino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(2) *N*-(4-chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-phenylethyl)(methyl)amino)methyl)-
15 7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(3) *N*-(4-Chlorobenzyl)-7-(2,3-dihydroxypropyl)-2-((((2*S*)-2-hydroxy-2-phenylethyl)(methyl)amino)methyl)-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(4) *N*-(4-chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-phenylethyl)(methyl)amino)methyl)-
20 7-(3-hydroxypropyl)-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(5) *N*-(4-Chlorobenzyl)-7-(2-hydroxyethyl)-2-((((2*S*)-2-hydroxy-2-phenylethyl)-(methyl)amino)methyl)-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(6) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-(3-methoxyphenyl)ethyl)(methyl)-amino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(7) *N*-(4-Chlorobenzyl)-7-ethyl-2-((((2*S*)-2-hydroxy-2-phenylethyl)(methyl)-amino)methyl)-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,
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(8) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-phenylethyl)(methyl)amino)methyl)-4-oxo-7-propyl-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(9) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-phenylethyl)(methyl)amino)methyl)-
30 7-(2-methoxyethyl)-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

(10) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-(4-cyanophenyl)ethyl)(methyl)-amino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,

- (11) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-(3-cyanophenyl)ethyl)(methylamino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,
- 5 (12) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-(4-(dimethylamino)phenyl)-2-hydroxyethyl)-(methylamino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,
- (13) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-(4-(hydroxymethyl)phenyl)ethyl)-(methylamino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide,
- 10 (14) *N*-(4-Chlorobenzyl)-2-((((2*S*)-2-hydroxy-2-(4-nitrophenyl)ethyl)(methylamino)methyl)-7-methyl-4-oxo-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxamide, or a pharmaceutically acceptable salt thereof.